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LaRosa(10) **Patent No.:** **US 7,566,539 B2**
(45) **Date of Patent:** **Jul. 28, 2009**(54) **ANTI-CCR2 ANTIBODIES AND METHODS OF USE THEREFOR**(75) Inventor: **Gregory J LaRosa**, Newton, MA (US)(73) Assignee: **Millennium Pharmaceuticals, Inc.**,
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(51) **Int. Cl.****G01N 33/53** (2006.01)**G01N 33/567** (2006.01)**G01N 33/574** (2006.01)**C07K 17/00** (2006.01)(52) **U.S. Cl.** **435/7.1; 435/7.2; 435/7.21; 435/7.23**(58) **Field of Classification Search** None
See application file for complete search history.(56) **References Cited****U.S. PATENT DOCUMENTS**

4,816,397	A	3/1989	Boss et al.	
4,816,567	A	3/1989	Cabilly et al.	
5,225,539	A	7/1993	Winter	
5,440,021	A	8/1995	Chuntharapai et al.	
5,543,503	A	8/1996	Chuntharapai et al.	
5,571,713	A	11/1996	Lyle et al.	
5,585,089	A	12/1996	Queen et al.	
5,657,277	A	8/1997	Shirley	
5,693,761	A	12/1997	Queen et al.	
5,693,762	A	12/1997	Queen et al.	
5,707,815	A	1/1998	Charo et al.	
5,808,960	A	9/1998	McClure	
5,858,089	A *	1/1999	Martinovic	118/13
5,859,205	A	1/1999	Adair et al.	
5,985,279	A	11/1999	Waldmann et al.	
6,006,339	A	12/1999	McClure	
6,075,181	A *	6/2000	Kucherlapati et al.	800/25
6,084,075	A *	7/2000	Lind et al.	530/388.22
6,312,689	B1	11/2001	LaRosa	
6,352,832	B1	3/2002	LaRosa et al.	
6,395,497	B1	5/2002	LaRosa	
6,406,694	B1	6/2002	LaRosa	
6,406,865	B2	6/2002	LaRosa	
6,448,021	B1	9/2002	LaRosa	
6,451,522	B2	9/2002	LaRosa	
6,458,353	B1	10/2002	LaRosa	
6,491,915	B2	12/2002	LaRosa	

6,696,550	B2	2/2004	LaRosa et al.
7,053,202	B2	5/2006	O'Keefe et al.
2003/0165494	A1	9/2003	LaRosa et al.
2004/0126851	A1	7/2004	LaRosa et al.
2004/0132980	A1	7/2004	LaRosa et al.
2004/0151721	A1	8/2004	O'Keefe et al.
2004/0265303	A1	12/2004	LaRosa et al.
2006/0147445	A1	7/2006	O'Keefe et al.

FOREIGN PATENT DOCUMENTS

WO	WO 91/09967	7/1991
WO	WO 94/09128	4/1994
WO	WO 94/12214	6/1994
WO	WO 95/08576	3/1995
WO	WO 95/19436	7/1995
WO	WO 97/31949	* 9/1997
WO	WO 97/47319	12/1997
WO	WO 98/42360	10/1998
WO	WO 98/44953	10/1998
WO	WO 99/15666	4/1999
WO	WO 00/05265	2/2000

OTHER PUBLICATIONS

Lederman et al. *Molecular Immunology*. 1991. 28;11:1171-1181.*
 Li et al. *PNAS*. 1980. 77;6:3211-3214.*
 Frade et al. *The Journal of Immunology* 1997, 159:5576-5584.*
 Li et al. *Biochemistry* 2000. 39:6296-6309.*
 Förster, R., et al., "A general method for screening mAbs specific for G-protein coupled receptors as exemplified by using epitope tagged BLR1-transfected 293 cells and solid-phase cell ELISA", *Biochemical and Biophysical Research Communications*, 196(3):1496-1503 (1993).
 Boring, L., et al., "Decreased lesion formation in CCR2^{-/-} mice reveals a role for chemokines in the initiation of atherosclerosis," *Nature*, 394(27):894-897 (1998).
 Ylä-Herttuala, S., et al., "Expression of monocyte chemoattractant protein 1 in macrophage-rich areas of human and rabbit atherosclerotic lesions," *Proc. Natl. Acad. Sci., USA*, 88:5252-5256 (1991).
 Taubman, M.B., et al., "JE mRNA Accumulates Rapidly in Aortic Injury and in Platelet-Derived Growth Factor-Stimulated Vascular Smooth Muscle Cells," *Circulation Research* 70(2): 314-325 (1992).
 Feng, A., et al., "Red Wine Inhibits Monocyte Chemotactic Protein-1 Expression and Modestly Reduces Neointimal Hyperplasia After Balloon Injury in Cholesterol-Fed Rabbits," *Circulation* 100:2254-2259 (1999).

(Continued)

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The present invention relates to an antibody or functional fragment thereof which binds to a mammalian (e.g., human) CC-chemokine receptor 2 (CCR2) or a portion of the receptor and blocks binding of a ligand to the receptor. The invention further relates to a method of inhibiting the interaction of a cell bearing mammalian CCR2 with a ligand thereof, and to use of the antibodies and fragments in therapeutic, prophylactic and diagnostic methods.

18 Claims, 15 Drawing Sheets